

In the Specification:

Page 8, the paragraphs on lines 2-7:

Figures 1A-1B show the DNA and deduced amino acid sequence of murine C140 receptor (SEQ ID NOS: 1 and 2, respectively).

Figures 2A-2B show the DNA and deduced amino acid sequence of human C140 receptor (SEQ ID NOS: 3 and 4, respectively).

Figure 3 shows a comparison of amino acid sequences for the human C140 receptor and murine C140 receptor (SEQ ID NOS: 6 and 5, respectively).

Page 9, the paragraphs on lines 1-6 and 14-25, respectively:

Figures 10A-10B show the nucleotide sequence and deduced amino acid sequence of a cDNA clone encoding murine C140 receptor (SEQ ID NOS: 60 and 61, respectively).

Figures 11A-11B show the nucleotide sequence and deduced amino acid sequence of a cDNA clone encoding human C140 receptor (SEQ ID NOS: 62 and 63, respectively).

The characteristics of the C140 receptor elucidated by the invention herein are summarized in Figures 1A/1B-4. Figures 1A-1B (SEQ ID NOS: 1 and 2) shows the complete DNA sequence of the clone encoding the murine receptor, along with the deduced amino acid sequence. As used herein, the "C140 receptor" refers to receptor in any animal species corresponding to the murine receptor contained in clone C140 described in Example 1 herein. Using the native DNA encoding the murine form of this receptor, the corresponding receptors in other species, including humans, as illustrated herein, may be obtained. Figures 2A-2B (SEQ ID NOS: 3 and 4) shows the corresponding DNA and deduced amino acid sequence of the human receptor.

Page 10, the paragraph on lines 3-5:

Figure 3 shows a comparison of the human and murine amino acid sequences (SEQ ID NOS: 6 and 5, respectively); as shown, these sequences exhibit a high degree of homology.

Page 10, line 20, through page 11, line 14:

Referring to Figure 5, similarities to the thrombin receptor are readily seen. Figure 5 compares the amino acid sequence of murine C140 with that of thrombin receptor. It is known that the thrombin receptor is activated by proteolytic cleavage of the Arg-Ser bond at positions 41 and 42, which releases an activation peptide that permits refolding of the receptor and activation via the newly created amino terminus. In an analogous manner, the C140 receptor is activated by cleavage of the Arg-Ser bond at positions 34 and 35, also liberating an activation peptide extending from position 1 of the putative mature protein to the cleavage site. It is believed that Arg-28 is the amino terminal amino acid residue of the mature protein, so the activation peptide has the sequence RNNSKGR (SEQ ID NO: 8). This peptide could thus be used as an index for activation of C140 receptor. In any event, the precise location of the N-terminus of the mature protein is unimportant for the design of agonists or antagonists. The activation peptide is likely to be freely filtered by the kidney and possibly concentrated in the urine and can be used as an index to activation of the C140 receptor.

Page 21, line 23, through page 22, line 8:

Preferred embodiments of AA₁ are Ser on 2,3-diaminopropionyl (2,3-diaP). Preferred embodiments of AA₂ and AA₃ are Val, Ile, Cha and Leu. Preferred embodiments for the residues in the remainder of the compound of formula (1) are those wherein AA₄ is Gly, AA₅ is Lys, Arg or Har, AA₆, if present, is Val, Ile, Cha or Leu, and AA₇, if present is Asp or Glu. Particularly preferred are compounds of formula (1) which are selected from the group consisting of SLIGRLETQPPIT (SEQ ID NO: 32), SLIGRLETQPPI (SEQ ID NO: 33), SLIGRLETQPP (SEQ ID NO: 34), SLIGRLETQP (SEQ ID NO: 35), SLIGRLETQ (SEQ ID NO: 36), SLIGRLET (SEQ ID NO: 37), SLIGRLE (SEQ ID NO: 38), SLIGRL (SEQ ID NO: 39), SLIGR (SEQ ID NO: 40), SLLGKVDGTSHVT (SEQ ID NO: 41), SLLGKVDGTSHV (SEQ ID NO: 42), SLLGKVDGTSH (SEQ ID NO: 43), SLLGKVDGTS (SEQ ID NO: 44), SLLGKVDGT (SEQ ID NO: 45), SLLGKVDG (SEQ ID NO: 46), SLLGKVD (SEQ ID NO: 47), SLLGKV (SEQ ID NO: 48), SLLGK (SEQ ID NO: 49), S(Cha)IGR (SEQ ID NO: 50), S(Cha)LGK (SEQ ID NO: 51), (2,3-diaP)-IGR (SEQ ID NO: 52), (2,3-diaP)LLGK (SEQ ID NO: 53), SLLGKR-NH₂ (SEQ ID NO: 54), SLIGRR-NH₂ (SEQ ID NO: 55), S(Cha)LGKK-NH₂ (SEQ ID NO: 56), S(Cha)IGRK-NH₂ (SEQ ID NO: 57), (2,3-diaP)-

LIGRK-NH₂ (SEQ ID NO: 58), (2,3-diaP)-LLGKK-NH₂ (SEQ ID NO: 59), and the amidated forms thereof.

Page 23, the paragraph on lines 16-21:

Particularly preferred among the antagonist peptides of this class are those selected from the group consisting of Mpr-LLGK (SEQ ID NO: 9), Mpr-LIGR (SEQ ID NO: 10), Mpr-(Cha)LKG (SEQ ID NO: 11), Mpr-(Cha)IGR (SEQ ID NO: 12), Mpr-LLGKK-NH₂ (SEQ ID NO: 13), Mpr-LIGRK-NH₂ (SEQ ID NO: 14), Mpr-LIGRKETQP-NH₂ (SEQ ID NO: 15), Mpr-LLGKKDGTS-NH₂ (SEQ ID NO: 16), (n-pentyl)₂-N-Leu-Ile-Gly-Arg-Lys-NH₂ (SEQ ID NO: 17) and (Me-N(n-pentyl)-Leu-Ile-Gly-Arg-Lys-NH₂ (SEQ ID NO: 18).

Page 24, the paragraph on lines 7-12:

Thus, peptides which contain the proteolytic region, namely, for example, SKGRSLIGRLET (SEQ ID NO: 19), the extracellular loops, such as those including ISYHLHGNNWVYGEALC (SEQ ID NO: 20); QTIYIPALNITTCHDVLPEEVLVGDMFNYFL (SEQ ID NO: 21); and HYFLIKTQRQSHVYA (SEQ ID NO: 22). The agonist peptides described below are also useful as immunogens.

Page 39, the paragraph on lines 16-27:

In one of the clones isolated (C140) the hybridizing region was localized to a 3.7 kb PstI fragment. This fragment was subcloned into the commercially available pBluescript vector. The hybridizing and adjacent regions were sequenced in both orientations by the Sanger chain termination method. Figure 1A-1B shows both the nucleotide sequence and the deduced amino acid sequence of the mouse C140 receptor (SEQ ID NOS: 1 and 2, respectively). The tentative signal sequence (SP) and the seven transmembrane regions are overlined, potential asparagine-linked glycosylation sites are marked with bold arrows, and the putative protease receptor cleavage site at Arg34-Ser35 is marked with an open arrow.

Page 40, the paragraphs on lines 3-13 and 27-29:

The availability of genomic DNA encoding the mouse protease C140 receptor permitted the retrieval of the corresponding human gene. A human genomic library cloned in the vector

EMBL3 was screened at exactly the conditions in Example 1 using the entire coding region of the murine clone as a probe. The recovered human gene including the DNA sequence and the deduced amino acid sequence (SEQ ID NOS: 3 and 4, respectively) are shown in Figure 2A-2B. Subsequent experiments indicated that the human C140 gene is located in the same region of the long arm of chromosome number 5 (5q12-5q13) as has been reported for the human thrombin receptor gene.

As shown in Figure 3, the deduced amino acid sequence of the human protease C140 receptor (SEQ ID NO: 6) shows extensive similarity (>90%) to the mouse sequence (SEQ ID NO: 5).

Page 41, the paragraph on lines 1-5:

Figure 5 shows an amino acid sequence alignment between the mouse C140 receptor (SEQ ID NO: 2) and the related G-protein receptor human thrombin receptor (SEQ ID NO: 7) (Coughlin, S. Cell). The tentative signal sequences (SP), transmembrane regions, and protease cleavage sites are marked.

Page 45, the table on lines 2-10:

<u>Peptide</u>	<u>Fold Increase in ⁴⁵Ca</u>
SLIGRL (<u>SEQ ID NO: 23</u>)	15
SLIGRA (<u>SEQ ID NO: 24</u>)	8.5
SLIGAL (<u>SEQ ID NO: 25</u>)	0
SLIARL (<u>SEQ ID NO: 26</u>)	4.3
SLAGRL (<u>SEQ ID NO: 27</u>)	0
SAIGRL (<u>SEQ ID NO: 28</u>)	0
ALIGRL (<u>SEQ ID NO: 29</u>)	1.3
SFFLRW (<u>SEQ ID NO: 30</u>)	1.7